

CLAIMS

What is claimed is:

1. An antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 5 protein.
- 5 2. The antibody or antigen-binding fragment thereof of Claim 1 wherein the mammalian CC-chemokine receptor 5 protein is a human CC-chemokine receptor 5 protein.
3. The antibody or antigen-binding fragment thereof of Claim 1 wherein the antibody is 5C7.
- 10 4. The antibody or antigen-binding fragment thereof of Claim 1 wherein the antibody or antigen-binding fragment thereof can compete with monoclonal antibody 5C7 for binding to a human CC-chemokine receptor 5 protein.
5. An antibody having specificity for a mammalian CC-chemokine receptor 5 protein, wherein the antibody inhibits binding of a ligand to the receptor and inhibits function associated with binding of the ligand to the receptor.
- 15 6. The antibody of Claim 5 wherein the ligand is human immunodeficiency virus.
7. An antigen-binding fragment of the antibody of Claim 3.

8. A method of inhibiting the interaction of a cell bearing mammalian CC-chemokine receptor 5 protein with a ligand thereof, comprising contacting said cell with an effective amount of an antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 5 protein.
- 5 9. The method of Claim 8 wherein the cell is selected from the group consisting of T cells, monocytes and cells comprising a recombinant nucleic acid encoding CCR5 or a portion thereof.
- 10 10. The method of Claim 9 wherein the T cells are selected from the group consisting of CD8+ cells, CD4+ cells and CD45RO+ cells.
- 10 11. The method of Claim 8 wherein the ligand is human immunodeficiency virus.
12. A method of inhibiting HIV infection of a cell, comprising contacting a cell with an effective amount of an antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 5 protein.
13. The method of Claim 12 wherein the cell is selected from the group consisting of T cells, monocytes and cells comprising a recombinant nucleic acid encoding CCR5 or a portion thereof.
- 15 14. The method of Claim 13 wherein the T cells are selected from the group consisting of CD8+ cells, CD4+ cells and CD45RO+ cells.
- 15 15. A method of treating HIV in a patient, comprising administering to the patient an effective amount of an antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 5 protein.
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16. A method of detecting expression of a mammalian CC-chemokine receptor 5 protein by a cell, comprising:
- 5 a) contacting a composition comprising a cell to be tested with an antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 5 protein under conditions appropriate for binding of said antibody or fragment thereto; and
- b) detecting binding of said antibody or fragment, wherein the binding of said antibody or fragment indicates the presence of said receptor on said cell.
- 10 17. The method of Claim 16 wherein the composition is a sample comprising human cells.
18. The method of Claim 16 wherein the antibody is 5C7.
19. A method of detecting the susceptibility of a mammal to HIV, comprising:
- 15 a) contacting a sample to be tested with an antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 5 protein under conditions appropriate for binding of said antibody or fragment thereto, wherein the sample comprises cells which express CCR5 in normal individuals; and
- b) detecting binding of said antibody or fragment, wherein the binding of said antibody or fragment indicates the level of receptor expressed by the cells, which correlates with the susceptibility of the mammal to HIV.
20. The method of Claim 19 wherein the composition is a sample comprising human cells.

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21. The method of Claim 19 wherein the antibody is 5C7.
22. A method of determining the prognosis for an HIV-infected mammal, comprising:
- 5 a) contacting a sample from the HIV-infected mammal to be tested with an antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 5 protein under conditions appropriate for binding of said antibody or fragment thereto, wherein the sample comprises cells which express CCR5 in normal individuals; and
- 10 b) detecting binding of said antibody or fragment, wherein the binding of said antibody or fragment indicates the level of receptor expressed by the cells, which correlates with a poorer prognosis for the HIV-infected mammal.
23. The method of Claim 22 wherein the composition is a sample comprising human cells.
- 15 24. The method of Claim 22 wherein the antibody is 5C7.
25. A method of inhibiting HIV infection in a patient, comprising administering to the patient an effective amount of an antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 5 protein.
- 20 26. A method of inhibiting leukocyte trafficking in a patient, comprising administering to the patient an effective amount of an antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 5 protein.

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27. The antibody or antigen-binding fragment thereof of Claim 1 wherein the antibody or antigen-binding fragment thereof binds a second extracellular loop or portion thereof of the mammalian CC-chemokine receptor 5 protein.
28. The antibody or antigen-binding fragment thereof of Claim 27 wherein the antibody is 2D7 or an antibody having an epitopic specificity which is the same as or similar to that of 2D7.
29. The antibody or antigen-binding fragment thereof of Claim 1 wherein the antibody or antigen-binding fragment thereof can compete with monoclonal antibody 2D7 for binding to a CC-chemokine receptor 5 protein.
30. The antibody of Claim 5, wherein the ligand is a chemokine.
31. The antibody of Claim 30, wherein the chemokine is selected from the group consisting of MIP-1 α , MIP-1 β , RANTES and combinations thereof.
32. An antigen-binding fragment of the antibody of Claim 28.
33. The method of Claim 8 wherein the ligand is a chemokine.
34. The method of Claim 33, wherein the chemokine is selected from the group consisting of MIP-1 α , MIP-1 β , RANTES and combinations thereof.
35. The method of Claim 12 wherein the antibody or antigen-binding fragment thereof is selected from the group consisting of 5C7, 2D7, an antigen binding fragment of 5C7, an antigen-binding fragment of 2D7, an antibody or antigen-binding fragment thereof having an epitopic specificity which is the same as or similar to that of 5C7, an antibody or antigen-binding fragment thereof having

an epitopic specificity which is the same as or similar to that of 2D7, and combinations of the foregoing.

36. The method of Claim 16 wherein the antibody or antigen-binding fragment thereof binds a second extracellular loop or portion thereof of the mammalian CC-chemokine receptor 5 protein.
37. The method of Claim 36 wherein the antibody is one or more antibodies selected from the group consisting of 2D7 and an antibody having an epitopic specificity which is the same as or similar to that of 2D7.
38. The method of Claim 19 wherein the antibody or antigen-binding fragment thereof binds a second extracellular loop or portion thereof of the mammalian CC-chemokine receptor 5 protein.
39. The method of Claim 38 wherein the antibody is one or more antibodies selected from the group consisting of 2D7 and an antibody having an epitopic specificity which is the same as or similar to that of 2D7.
40. The method of Claim 22 wherein the antibody binds a second extracellular loop or portion thereof of the mammalian CC-chemokine receptor 5 protein.
41. The method of Claim 40 wherein the antibody is one or more antibodies selected from the group consisting of 2D7 and an antibody having an epitopic specificity which is the same as or similar to that of 2D7.
42. The method of Claim 25 wherein the antibody is selected from the group consisting of 5C7, 2D7, an antigen-binding fragment of 5C7, an antigen-binding fragment of 2D7, an antibody or antigen-binding fragment thereof having an

epitopic specificity which is the same as or similar to that of 5C7, an antibody or antigen-binding fragment thereof having an epitopic specificity which is the same as or similar to that of 2D7, and combinations of the foregoing.

43. A method of inhibiting the interaction of a cell bearing mammalian CC-chemokine receptor 5 protein with a chemokine, comprising contacting said cell with an effective amount of an antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 5 protein.
44. The method of Claim 43 wherein the antibody or antigen-binding fragment thereof is selected from 2D7, an antigen-binding fragment of 2D7, an antibody or antigen-binding fragment thereof having an epitopic specificity which is the same as or similar to 2D7, and combinations of the foregoing.
45. A method of inhibiting a function associated with binding of a chemokine to a mammalian CC-chemokine receptor 5 protein or antigen-binding fragment thereof, comprising contacting a composition comprising the protein with an effective amount of an antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 5 protein.
46. The method of Claim 45 wherein the antibody or antigen-binding fragment thereof is selected from 2D7, an antigen-binding fragment of 2D7, an antibody or antigen-binding fragment thereof having an epitopic specificity which is the same as or similar to that of 2D7, and combinations of the foregoing.
47. The hybridoma cell line deposited under ATCC Accession No. HB-12366.
48. The hybridoma cell line deposited under ATCC Accession No. HB-12222.

49. A monoclonal antibody produced by the hybridoma cell line of Claim 47 or an antigen-binding fragment thereof.
50. A monoclonal antibody produced by the hybridoma cell line of Claim 48 or an antigen-binding fragment thereof.
- 5 51. A test kit for use in detecting the presence of a mammalian CC-chemokine receptor 5 protein in a biological sample comprising
- a) an antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 5 protein; and
 - b) one or more ancillary reagents suitable for detecting the presence of a
- 10 complex between said antibody or antigen-binding fragment thereof and said protein.
52. The kit of Claim 51, wherein the antibody or antigen-binding fragment thereof is selected from 5C7, 2D7, an antigen-binding fragment of 2D7, an antigen-binding fragment of 5C7, an antibody or antigen-binding fragment thereof
- 15 having an epitopic specificity which is the same as or similar to that of 5C7, an antibody or antigen-binding fragment thereof having an epitopic specificity which is the same as or similar to that of 2D7, and combinations of the foregoing.
53. A method according to Claim 15, wherein the antibody is 5C7 or 2D7.
- 20 54. A method according to Claim 26, wherein the antibody is 5C7 or 2D7.
55. A bispecific antibody or antigen-binding fragment thereof having an epitopic specificity which is the same as or similar to that of 2D7 and 5C7.

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56. A bispecific antibody or antigen-binding fragment thereof which binds a second extracellular loop or portion thereof and an amino terminal region or portion thereof of a mammalian CC-chemokine receptor 5 protein .
57. A method of detecting or identifying an agent which binds a mammalian CC-chemokine receptor 5 protein or ligand binding variant thereof, comprising combining
- an agent to be tested;
- an antibody or antigen-binding fragment selected from the group consisting of monoclonal antibody 2D7, an antibody having an epitopic specificity which is the same as or similar to that of 2D7, and antigen-binding fragments thereof; and
- a composition comprising a mammalian CC-chemokine receptor 5 protein or a ligand binding variant thereof,
- under conditions suitable for binding of said antibody or antigen-binding fragment thereto, and
- detecting or measuring binding of said antibody or fragment to said mammalian CC-chemokine receptor 5 protein or ligand binding variant.
58. The method of Claim 57, wherein the formation of a complex between said antibody or fragment and said mammalian CC-chemokine receptor 5 protein or variant is monitored, and wherein a decrease in the amount of complex formed relative to a suitable control is indicative that the agent binds said receptor or variant.
59. The method of Claim 57, wherein the composition comprising a mammalian CC-chemokine receptor 5 protein or a ligand binding variant thereof is a membrane fraction of a cell bearing recombinant CC-chemokine receptor 5 protein or ligand binding variant thereof.

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60. The method of Claim 57, wherein the antibody is labeled with a label selected from the group consisting of a radioisotope, spin label, antigen label, enzyme label, fluorescent group and chemiluminescent group.
- 5 61. The method of Claim 57, wherein the agent is an antibody having specificity for a CC-chemokine receptor 5 protein or antigen-binding fragment thereof.
62. A method of detecting or identifying an agent which binds a mammalian CC-chemokine receptor 5 protein or a ligand binding variant thereof comprising combining
- 10 an agent to be tested;
- an antibody or antigen binding fragment selected from the group consisting of monoclonal antibody 2D7, an antibody having an epitopic specificity which is the same as or similar to that of 2D7, and antigen-binding fragments thereof; and
- 15 a cell bearing a mammalian CC-chemokine receptor 5 protein or a ligand binding variant thereof,
- under conditions suitable for binding of said antibody or antigen-binding fragment thereto, and
- detecting or measuring binding of said antibody or fragment to said mammalian CC-chemokine receptor 5 protein or variant.
- 20 63. The method of Claim 62, wherein the formation of a complex between said antibody or fragment and said mammalian CC-chemokine receptor 5 protein or variant is monitored, and wherein a decrease in the amount of complex formed relative to a suitable control is indicative that the agent binds said receptor or variant.

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64. The method of Claim 62, wherein the antibody is labeled with a label selected from the group consisting of a radioisotope, spin label, antigen label, enzyme label, fluorescent group and chemiluminescent group.
65. The method of Claim 62, wherein the agent is an antibody having specificity for a CC-chemokine receptor 5 protein or antigen-binding fragment thereof.
66. A method of detecting a mammalian CC-chemokine receptor 5 protein, comprising:
- a) contacting a sample to be tested with an antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 5 protein under conditions appropriate for specific binding of said antibody or antigen-binding fragment thereto; and
 - b) detecting or measuring binding of said antibody or antigen-binding fragment thereof, wherein the binding of said antibody or antigen-binding fragment thereof to material in said sample is indicative of the presence of a mammalian CC-chemokine receptor 5 protein in said sample.
67. The method of Claim 66, wherein the antibody or antigen-binding fragment thereof is selected from the group consisting of 2D7, an antigen-binding fragment of 2D7, and an antibody or antigen-binding fragment thereof having an epitopic specificity which is the same as or similar to that of 2D7.
68. The method of Claim 66, wherein the sample is a cellular fraction which comprises a mammalian CC-chemokine receptor 5 protein or portion thereof in normal individuals.
69. A method of detecting the susceptibility of a mammal to HIV, comprising:

- 5 a) contacting a sample to be tested with an antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 5 protein under conditions appropriate for binding of said antibody or antigen-binding fragment thereto; and
- 5 b) detecting or measuring binding of said antibody or antigen-binding fragment thereof,

wherein the binding of said antibody or antigen-binding fragment thereof to material in said sample is indicative of the level of a mammalian CC-chemokine receptor 5 protein in said sample, which is correlated with the susceptibility of the mammal to HIV.

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70. A method of inhibiting a function associated with binding of a chemokine to the CC-chemokine receptor 5 protein in a mammal in need thereof, comprising administering an effective amount of an antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 5 protein.

- 15 71. A method of treating a CC-chemokine receptor 5-mediated condition in a patient, comprising administering to the patient an effective amount of an antibody or antigen-binding fragment thereof which binds to mammalian CC-chemokine receptor 5.

- 20 72. A method according to Claim 71, wherein said CC-chemokine receptor 5-mediated condition is arthritis.

73. A method according to Claim 72, wherein said CC-chemokine receptor 5-mediated condition is rheumatoid arthritis.

74. A method according to Claim 72, wherein said CC-chemokine receptor 5-mediated condition is juvenile rheumatoid arthritis.

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